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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
DIBRINO, MARIANNE NMN	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 02/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/461,684	LAUS ET AL.	
	Examiner	Art Unit	
	DiBrino Marianne	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *1/30/02, 9/29/03, 4/8/02*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-7* is/are pending in the application.

4a) Of the above claim(s) *3* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 4-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's amendments filed 1/30/02, 9/29/03 and 4/8/02 are acknowledged and have been entered.

Claims 1 and 4-7 are pending. It is noted that Applicant canceled claims 2, 3 in the amendment filed 1/30/02 and claims 8-18 in the amendment filed 1/2/01.

2. Applicant is reminded of Applicant's election of Group I (claims 1-7) and species of SEQ ID NO: 6.

Claims 1 and 4-7 read on the elected species, SEQ ID NO: 6.

Claims 1 and 4-7 are currently being examined to the extent they read upon the elected species SEQ ID NO: 6.

The following are new grounds of rejection necessitated by Applicant's amendments filed 1/30/02, 9/29/03 and 4/8/02.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1 and 4-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description or me claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter" , Vas-Cath. lnc. V. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the applicant had possession at the time of invention of the claimed using a composition comprising an antigen comprising an added peptidic sequence that is not one or more of SEQ ID NO: 1-9 (i.e., that does not consist of one or more of SEQ ID NO: 9) that facilitates entry of the said antigen into APC, and including compositions comprising antigens specific to tumors or pathogens, such as antigens specific to HIV and cancer antigens.

The instant claims encompass a composition comprising an antigen having an added peptidic sequence, said added peptidic sequence comprising SEQ ID NO: 10 which is SIINFEKL, a peptide disclosed on page 17 beginning on line 5, to be an imunogenic peptide rather than a peptide that facilitates entry of an antigen into APC. The instant claims also encompass a composition comprising an antigen comprising one of SEQ ID NO: 1-10 and comprising an added peptidic sequence that facilitates entry of said antigen into APC that is not one of SEQ ID NO: 1-10, i.e., "comprising one or more sequences selected from the group consisting of" SEQ ID NO: 1-10, but does not specify that the *said* added peptidic sequence that facilitates entry of said antigen into APC consists of one of SEQ ID NO: 1-10. The instant claims encompass said added peptidic sequence that comprises one of SEQ ID NO: 1-10 but may include additional undisclosed sequences. The said antigen is disclosed to be capable of eliciting an enhanced CTL response in the context of MHC class I. There is insufficient disclosure on such a composition.

The specification discloses, in the paragraph spanning pages 5 and 6, that CTL are induced when a protein enters the MHC class I pathway of cytosolic antigen processing in an APC. The specification further discloses, in the paragraph spanning pages 6 and 7, that the typical response to soluble protein antigens is a Class II MHC mediated response, and that the compositions of the present invention allow soluble protein antigens to enter the Class I pathway which is typically reserved for foreign cellular antigens. The specification further discloses that peptidic sequences such as those represented by one or more of SEQ ID NO: 1-9 are linked to an antigen, the antigen is capable of triggering naive CTL responses in vivo, and is more efficient in stimulating corresponding Class I restricted memory T cells in vitro (page 7 at lines 19-36).

In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. However, a generic statement such as "added peptidic sequence'' that is not one of SEQ ID NO: 1-9 without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by the property of facilitating entry of the antigen into APC. lt does not specifically define any of the added peptidic sequences that provide the function of facilitating entry into APC. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by the said property of facilitating entry of an antigen into an APC does not suffice to define the genus because it is only an indication of what the property the added peptidic sequence'' has. See Fiers, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06. It is only a definition of a useful result rather than a definition of what achieves that result. Many such species may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d

1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does ''little more than to outlin (el goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate. ''). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.

The instant disclosure of a few species or subgenera of "added peptidic sequence'' does not adequately describe the scope of the claimed genus. Structural features that distinguish members of the genus from others excluded are missing from the disclosure. Because of this lack of disclosure of sufficient relevant identifying characteristics and because the genus is highly variant, the disclosure is insufficient to describe the genus.

Applicant's arguments in the amendment filed 4/8/02 are moot in light of the new rejection set forth supra.

5. Claims 1 and 4-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification while being enabling for making and/or using a composition comprising an antigen and an added peptidic sequence which facilitates entry of an antigen into APC that consists of one or more of SEQ ID NO: 1-9 for the purpose of eliciting an enhanced CTL response, does not reasonably provide enablement for making and/or using a composition comprising an added peptidic sequence that is one or more of SEQ ID NO: 1-10.

The instant claims encompass a composition comprising an antigen having an added peptidic sequence comprising SEQ ID NO: 10 which is SIINFEKL, a peptide disclosed on page 17 beginning on line 5, to be an imunogenic peptide rather than a peptide that facilitates entry of an antigen into APC. The instant claims also encompass a composition comprising an antigen comprising one of SEQ ID NO: 1-10 and an added peptidic sequence that facilitates entry of said antigen into APC that is not one of SEQ ID NO: 1-10, i.e., "comprising one or more sequences selected from the group consisting of" SEQ ID NO: 1-10, but does not specify that the *said* added peptidic sequence that facilitates entry of said antigen into APC consists of one or more of SEQ ID NO: 1-10. The instant claims also encompass a composition comprising an antigen specific for a tumor or antigen, including HIV, and an intended use in immunizing a subject against a tumor or pathogen such as a vaccine for HIV or cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The specification does not disclose how to make and/or use the instant invention wherein the added peptidic sequence is not one or more of SEQ ID NO: 1-9. The claimed composition comprises any added peptidic sequence with the property of facilitating entry of an antigen into APC, including those consisting of one or more of SEQ ID NO: 1-10. The specification has not enabled the breadth of the claimed invention in view of the teachings of the specification because the claims encompass a composition comprising added peptidic sequences, said added

peptidic sequences not consisting of one or more of SEQ ID NO: 1-9. The state of the art is such that it is unpredictable in the absence of appropriate evidence whether the claimed composition can be made and/or used. The specification discloses no working examples that are not comprised of SEQ ID NO: 1 and SEQ ID NO: 2.

The specification discloses, in the paragraph spanning pages 5 and 6, that CTL are induced when a protein enters the MHC class I pathway of cytosolic antigen processing in an APC. The specification further discloses, in the paragraph spanning pages 6 and 7, that the typical response to soluble protein antigens is a Class II [MHC] mediated response, and that the compositions of the present invention allow soluble protein antigens to enter the Class I pathway which is typically reserved for foreign cellular antigens. The specification further discloses that peptidic sequences such as those represented by one or more of SEQ ID NO: 1-7 or those disclosed on page 7 at lines 29-36 are linked to an antigen, the antigen is capable of triggering naive CTL responses in vivo, and is more efficient in stimulating corresponding Class I restricted memory T cells in vitro (page 7 at lines 19-36).

Evidentiary references Osicka et al (Inf. Immun. 86/1: 247-256, 2000, Abstract) and Guermonprez et al (J. Immunol. 162/4: 1910-1916, 1999, Abstract) teach OVA antigen with added peptidic sequence from ACT-Hly which delivers the antigen into the MHC class I antigen processing pathway.

In view of the lack of predictability of the art to which the invention pertains, undue experimentation would be required to make and/or use "added peptidic sequences" which are not one or more of SEQ ID NO: 1-7 or one of the sequences disclosed on page 7 at lines 29-36 of the instant specification. The enablement provided by the specification is not commensurate with the scope of the claims.

Applicant's arguments in the amendment filed 4/8/02 are moot in light of the new rejection set forth supra.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1 and 4-7 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Buschle et al (PNAS USA 94: 3256-3261, 4/1997, IDS reference) in view of Kim et al (J. Immunol. 159(4): 1666-1668, 8/1997).

During patent examination, the pending claims must be "given the broadest reasonable interpretation consistent with the specification." Applicant always has the opportunity to amend the claims during prosecution and broad interpretation by the examiner reduces the possibility that the claim, once issued, will be interpreted more broadly than is justified. In re Prater, 162 USPQ 541, 550 - 51 (CCPA 1969)

The instant claims also encompass a composition comprising an antigen comprising one of SEQ ID NO: 1-10 and an added peptidic sequence that facilitates entry of said antigen into APC that is not one of SEQ ID NO: 1-10, i.e., "comprising one or more sequences selected from the group consisting of" SEQ ID NO: 1-10, but does not specify that the *said* added peptidic sequence that facilitates entry of said antigen into APC is one of SEQ ID NO: 1-10. Therefore, the instant claims read upon compositions comprising antigens and an added peptidic sequence that facilitates entry of antigen into APC, said added peptidic sequence being other than SEQ ID NO: 1-10.

Buschle et al teach that polycationic amino acids have been employed to enhance transport of proteins into cells and teach the ability of different cationic polymers, two of which are poly-Arg and poly-Lys, to transfer peptides to APCs (especially Abstract). Buschle et al teach compositions comprising antigenic peptides from pathogens and tumors and poly-Lys or poly-Arg (especially Abstract, Table 1 and page 3258, column 2 first full paragraph).

Buschle et al do not teach a composition comprising an antigen having an added peptidic sequence, wherein the added peptidic sequence is linked to the said antigen, nor wherein the antigen-polycationic sequence is a fusion protein.

Kim et al teach that because exogenous proteins do not ordinarily enter the cytosol [of APC] and access the MHC class I-processing pathway, protein-based vaccines that induce class I-restricted CTL responses have proved difficult to design. Kim et al further teach that they have addressed this problem by conjugating OVA antigen to a cationic peptide derived from HIV-1 tat which has a cysteine at the carboxy terminal end, and teach administration of a composition comprising the antigen/cationic peptide to APC leads to processing and presentation of the peptides in association with Class I MHC (especially Abstract).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have made an N-terminal cysteinylated peptide (as taught by Kim et al) version of the cationic poly-Lys or the poly-Arg peptide taught by Buschle et al to have conjugated it to one of the antigens taught by Buschle et al or Kim et al as taught by Kim et al for the antigen/cationic peptide of Kim et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to do this to enhance the transport of proteins or peptides from pathogens or tumors into the class I processing pathway and to stimulate CTL responses because Kim et al teach that protein-based vaccines that induce class I-restricted CTL responses have proved difficult to design and conjugation of an antigen to a cationic peptide leads to class I MHC processing and presentation, Buschle et al teach that polycationic amino acids have been employed to enhance transport of proteins into cells, they teach the ability of different cationic polymers, two of which are poly-Arg and poly-Lys, to transfer peptides to APCs and they teach compositions comprising antigenic peptides from pathogens or tumors and poly-Lys or poly-Arg. The instant claims 4-7 are included in this rejection because SEQ ID NO: 6 is poly-Arg or poly-Lys, and it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used any length poly-Lys or poly-Arg that was effective. Claim 6 is included in this rejection because claimed recitation of intended use in immunizing a subject against a tumor or pathogen wherein the antigen is specific to the tumor or antigen does not carry any patentable weight per se. A compound is the same compound irrespective of its intended use. Claim 7 is included in this rejection because the recitation of a method wherein the claimed product is made carries no patentable weight in this product claim.

Applicant's arguments in the amendment filed 4/8/02 have been fully considered but are not persuasive.

Applicant's position is of record in the said amendment.

It is the Examiner's position that Buschle et al do teach compositions comprising antigenic peptides from pathogens and tumors and poly-Lys or poly-Arg, i.e., comprising an antigenic peptide the "added peptidic sequence" (especially Abstract, Table 1 and page 3258, column 2 first full paragraph) as enunciated supra in the instant rejection. It is the Examiner's further position that Applicant is arguing Buschle et al and Kim et al separately. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See in re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

It is the Examiner's position that Buschle et al teach use of polycationic amino acid sequences including poly Lys and poly Arg to enhance transport of antigenic tumor associated peptides into APC for induction of an effective anticancer immune response, that response being almost exclusively presented in context of MHC class I, i.e., for generation of a CTL response (especially column 1 on page 3256). SEQ ID NO: 6 of the instant claims is N-terminal cysteinylated poly Arg or poly Lys. In addition, as discussed supra, the claim language is not limited to one of SEQ ID NO: 1-9 as the added peptidic sequence. It is the Examiner's further position that Kim et al teach administration of an antigenic peptide coupled to an N-cysteinlyated cationic peptide for facilitation of the antigenic peptide into the Class I MHC

processing and presentation pathway. In addition with regard to the poly Lys and poly Arg taught by Buschle et al, the claimed SEQ ID NO: 6 appears to be the same or similar to the added peptidic sequence of the prior art absent a showing of unobvious differences. Since the Patent Office does not have the facilities for examining and comparing the composition of the instant invention to those of the prior art, the burden is on applicant to show an unobvious distinction between the antibody of the instant invention and that of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

8. No claim is allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday and Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Chan Y Christina, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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